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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/486,094	07/17/2000	GEORGES ` FREYSSINET	A33002-PCT	1744

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EXAMINER
KUBELIK, ANNE R

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 02/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/486,094	FREYSSINET ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- Th MAILING DATE of this communication appears on the cover she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 September 2002 and 18 November 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-42* is/are pending in the application.

4a) Of the above claim(s) *11-18 and 36-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-10,19-30 and 41-42* is/are rejected.

7)☒ Claim(s) *31-35,39 and 40* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *17* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-3 have been cancelled, claims 4-10, 19-35 and 39 have been amended, and claims 40-42 have been added, as requested in Paper No.16, filed 23 September 2002. Claims 4-42 are pending.

2. This application contains claims 11-18 and 36-38 drawn to an invention nonelected without traverse in Paper No. 12. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01. Claims 4-10, 19-35 and 39-42 are examined.

3. The substitute specification filed 23 September 2002 has not been entered, as the first page of the substitute specification is numbered "2" instead of "1". A replacement substitute specification is required. it is not necessary to send a new marked-up copy of the specification, unless new amendments are included, and a copy of the claims should be not be included.

4. The draftsman has approved the drawings filed 23 September 2002.

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Sequence Rules

6. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825.

A sequence identifiers is missing from claim 8, line 4.

Full compliance with the sequence rules is required in response to this Office action. A complete response to this Office action must include both compliance with the sequence rules and a response to the issues set forth below. Failure to fully comply with both of these requirements in the time period set for in this Office action will be held to be non-responsive.

Response to Amendment

7. The rejection of claims 1-10 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter is WITHDRAWN in light of amendment to of cancellation of the claims.

Claim Objections

8. Claims 31-35 and 39-40 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

9. Claims 4, 9-10 and 19 are objected to because of the following informalities:

There is an improper article before "nucleic" in claim 19, line 2.

In claim 4, line 3, claim 9, line 2 and claim 10, lines 2-3, "SEQ ID NO.:" should be replaced with --SEQ ID NO:--.

Claim Rejections - 35 USC § 112

10. Claims 4-10, 19-30 and 41-42 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection is repeated for the reasons of record as set forth in the Office action mailed 22 April 2002, as applied to claims 1-10, 19-35 and 39. Applicant's arguments filed 23 September 2002 have been fully considered but they are not persuasive.

Applicant urges that the claims have been amended to remove all references to androctonine and points to the definitions of protein and DNA homology in the specification (response pg 38-39).

This is not found persuasive because the specification does not describe DNA molecules other than SEQ ID NO:1 encompassed by the claims. The structural features that distinguish all such nucleic acids from other nucleic acids are not provided. The specification does not teach the structural features of the nucleic acids that encode proteins of general formula (I) and does not teach the structural features of nucleic acids that are homologous to SEQ ID NO:1.

Additionally, the claims lack written description because the function of the protein encoded by the claimed nucleic acid is not recited in the claim.

11. Claims 4-10, 19-30 and 41-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding an androctonine of SEQ ID NO:2, a chimeric gene, vector, transformed bacterium and plant comprising the nucleic acid, and method of transformation of tobacco with the nucleic acid operably linked to a PR-1a signal peptide coding sequence, does not reasonably provide enablement for nucleic acids encoding a protein of general formula (I) and plants transformed with those nucleic acids. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly

connected, to make and/or use the invention commensurate in scope with these claims. The rejection is slightly modified from the rejection of record as set forth in the Office action mailed 22 April 2002, as applied to claims 1-10, 19-35 and 39, due to amendment of the claims. Applicant's arguments filed 23 September 2002 have been fully considered but they are not persuasive.

The claims are broadly drawn to a multitude of nucleic acids encoding any protein of general formula (I), nucleic acids encoding homologues of SEQ ID NO:2, or nucleic acids that are homologous to SEQ ID NO:1, a method of transforming a multitude of host organisms with those nucleic acids, and host organisms so obtained.

The instant specification, however, only provides guidance for a nucleic acid construct encoding the PR-1a signal sequence from tobacco fused to an androctonine coding sequence (SEQ ID NO:1) and plant and *Agrobacterium* transformation vectors comprising the construct (example 1), and transformation of tobacco and testing the transformed tobacco for tolerance to the herbicide bromoxynil (example 2).

The instant specification fails to provide guidance for any nucleic acids encoding a protein of general formulary (I), other than SEQ ID NO:1, for nucleic acids encoding homologues of SEQ ID NO:2, or for nucleic acids that are homologous to SEQ ID NO:1. The instant specification also fails to provide guidance for transformation of a yeast or fungus. The specification also fails to provide guidance for producing fungal-resistant plants. Lastly, the specification fails to provide guidance for expression of the protein encoded by SEQ ID NO:1, which has no starting methionine, without attaching a signal peptide.

Making "conservative" substitutions (*e.g.*, substituting one polar amino acid for another, or one acidic one for another) does not produce predictable results. Lazar et al (1988, Mol. Cell. Biol. 8:1247-1252) showed that the "conservative" substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while "nonconservative" substitutions with alanine or asparagine had no effect (abstract). Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach that when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the "nonconservative" amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the "conservative" amino acid arginine drastically reduced enzyme activity (see Table 1). All these mutated proteins, however, would be "homologous peptides" of the original protein.

Given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate nucleic acids encoding homologues of the protein of SEQ ID NO:1. Making all possible single amino acid substitutions in an 25 amino acid long protein like that encoded by SEQ ID NO:1 would require making and analyzing 19^{25} nucleic acids. Because nucleic acids encoding homologues of the protein of SEQ ID NO:2, *i.e*, proteins with 65% identity to SEQW ID NO:2, would have 8 amino acid substitutions, many more nucleic acids than 19^{25} would need to be made and analyzed.

Expressing pesticidal peptides in plants is also unpredictable. Okamoto et al (1998, Plant Cell Physiol. 39:57-63) transformed tobacco plants with a gene encoding a short antimicrobial peptide behind a constitutive promoter. The peptide was so unstable in plants that it could not be

detected, even though the mRNA encoding it was expressed at high levels (pg 59, left column, last paragraph, to pg 60, entire left column). Similarly, Allefs et al (1995, Am. Potato J. 72:437-445) teach that potato plants transformed with a gene encoding the antimicrobial peptide cecropin B degrade the peptide and have no increase in resistance to infection (pg 441-443).

Even when peptides are not degraded in the transgenic plants, they unexpectedly do not retain their biological activity. Peptides that are effective pesticides when isolated and contacted with microorganisms or fed to insects do not function as pesticides when genes encoding them are transformed into plants. When tobacco plants were transformed with a gene encoding cecropin B, the transformed plants displayed no increase in disease resistance (Hightower et al, 1994, Plant Cell Rep. 13:295-299, see pg 297, paragraph spanning the columns, to pg 298, right column, paragraph 1). De Bolle et al (1996, Plant Mol. Biol. 31:993-1008) teach that tobacco plants transformed with genes encoding seed antimicrobial peptides had no increase in resistance to infection (pg 1004, paragraph spanning the columns). Lastly, Pang et al (1992, Gene 116:165-172) teach that in tobacco plants transformed with a gene encoding the scorpion insectotoxin I_5A, the peptide is not correctly processed and the resulting plants had no paralytic effect on tobacco budworm (pg 170, right column).

Not all proteins of general formula (I) are androctonines. Cheuk et al (1996, Genbank Accession No. AC003981) and Carlson et al (1996, Genbank Accession No. K02672) each teach an isolated nucleic acid that encodes a protein of general formula (I). The protein taught by Cheuk et al is a violaxanthin de-epoxidase and that taught by Carlson et al is a ribonucleoside diphosphate reductase. The specification does not teach how to use nucleic acids encoding these

proteins. It is unlikely that plants transformed with either of these nucleic acids would be pathogen-resistant.

As the specification does not describe the production of fungus-resistant plants that have been transformed with a nucleic acids encoding any protein of general formula (I), nucleic acids encoding homologues of SEQ ID NO:2, or nucleic acids that are homologous to SEQ ID NO:1, undue trial and error experimentation would be required to screen through the myriad of nucleic acids encompassed by the claims and plants transformed therewith, to identify those with fungus-resistance, if such plants are even obtainable.

Applicant urges that the amendments to the claims obviate the basis for this rejection. Applicant argues that transformation of yeasts and fungi are well-known to those of ordinary skill in the art and cites Thompson et al, Lorito et al and Robinson et al. Applicant has deleted all reference to baculovirus transformation. Applicant urges that the amendments to the claims make them enabled for producing fungal-resistant plants and cites Oldach et al, Gao et al and Mitsuhara et al as evidence as to the level of skill in the art with respect to the creation of fungus resistant plants through the introduction of a heterologous transgene. Applicant thus argues it would not be undue experimentation to create such plants. With respect to the allegation that the specification fails to provide guidance for expression of the protein encoded by SEQ ID NO:1, which has no starting methionine, without attaching a signal peptide, Applicant argues that claims 4-10 are directed to a nucleic acid encoding a protein of general formula (I), and none of the claims are directed to the expression product of the nucleic acid fragment; thus the presence of the initiating methionine is irrelevant to the validity of the claims. Applicant also urges that a

signal peptide was used in example 1 and in claims 12-17 drawn to a non-elected invention (response pg 39-42).

Thompson et al (1998) teach an improved protocol for transformation of yeast by electroporation, Lorito et al (1993) teach biolistic transformation of two fungal species, and Robinson et al (1999) teach transformation of a fungus by electroporation. Oldach et al (2001) teach production of fungal resistant wheat by transformation with a nucleic acid encoding a 94-amino acid long antifungal protein from *Aspergillus*, Gao et al (2000) teach production of fungal resistant potato by transformation with a nucleic acid encoding a 72-amino acid long antifungal protein from alfalfa, and Mitsuhara et al (2000) teach production of fungal and bacterial resistant tobacco by transformation with a nucleic acid encoding sarcotoxin IA, a 64-amino acid long protein.

This is not found persuasive.

None of Thompson et al (1998), Robinson et al (1999), Oldach et al (2001), Gao et al (2000), or Mitsuhara et al (2000) can be relied on for enablement. See *In re Glass*, 181 USPQ 31, 34 (CCPA 1974), which teaches that references published after the filing date of an application may not be relied upon for the enablement of the specification.

With respect to Applicant's arguments that it would be within the skill of one in the art to produce fungus-resistant plants with the claimed nucleic acid, Examiner disagrees. The specification does not teach how to make or isolate nucleic acids encoding proteins of general formula (I), nucleic acids encoding homologues of SEQ ID NO:2, or nucleic acids that are homologous to SEQ ID NO:1. Lazar et al and Hill et al, cited in the prior Office action, teach that making substitutions in a protein, even conservative substitutions, is unpredictable.

There are 19^{21} nucleic acids that encode a protein that is the same length as SEQ ID NO:2 and that have general formula (I). The claims are drawn to nucleic acids encoding many more proteins than that, some longer that SEQ ID NO:2 and some shorter. As discussed above, not all proteins of general formula (I) are androctonines, and are unlikely to provide fungal resistance to any plant. Undue experimentation would thus be required to screen through all the nucleic acids encompassed by the claims to find one those provide fungal resistance to plants.

Applicant has not even demonstrated that any plant transformed with SEQ ID NO:1 is more resistant to fungal pathogens than non-transformed plants. Applicant is invited to submit a Declaration providing data showing that.

Even if the publication dates of Oldach et al (2001), Gao et al (2000), and Mitsuhara et al (2000) did not preclude their use to support enablement of the instant claims, they would not do so. All the proteins in those papers are much longer than the 25 amino acid long protein encoded by SEQ ID NO:1.

Each of Okamoto et al, De Bolle et al, and Pang et al, cited in the prior Office action and above, all teach that when plants were transformed with nucleic acids encoding antimicrobial peptides closer in length to the 25 amino acid long androctonin, *i.e.* proteins 26-39 amino acids long, the peptide was degraded, incorrectly processed or did not provide resistance.

With respect to Applicant's arguments about the requirement for a signal peptide, *i.e.*, that claims 4-10 are directed to a nucleic acid encoding a protein of general formula (I), and none of the claims are directed to the expression product of the nucleic acid fragment and that a signal peptide was used in example 1 and in claims 12-17 drawn to a non-elected invention, Examiner disagrees.

In order for nucleic acids encoding a protein of general formula (I) provide any function to a plant, whether it be fungal resistance or to simply produce the protein a plant, the protein needs to have a starting methionine. The protein encoded by the nucleic acid of claim 7, for example, lacks this methionine. Thus, without that methionine this nucleic acid would not be able to encode a protein in the host organisms of claims 28-30. Thus, the presence of the initiating methionine is very relevant to the validity of the claims. That a signal peptide was used in the exemplified constructs points to its necessity.

12. Claims 6, 9-10, 19-30 and 41-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections. The rejection is repeated for the reasons of record as set forth in the Office action mailed 22 April 2002, as applied to claims 3-10, 19-35 and 39. Applicant's arguments filed 23 September 2002 have been fully considered but they are not persuasive.

Applicant urges that the claims have been amended (response pg 42-43). This is not found persuasive because the following rejections remain or are new, due to amendment of the claims:

Claim 6 lacks antecedent basis for the limitation "the basic amino acids" in line 2. Additionally, asparagine and homoasparagine are not basic amino acids.

Claim 9 lacks antecedent basis for the limitation "The isolated nucleic acid fragment" in line 1.

Claim 9 is indefinite in its recitation of "nucleic acid fragment comprising the nucleic acids encoding ... SEQ ID NO:2". Does Applicant intend that the isolated nucleic acid fragment comprise in that fragment ALL the multitude of nucleic acids that can encode SEQ ID NO:2?

Claim 9 remains indefinite in its recitation of "homologous peptide sequences". The definition on page 5, lines 5-17, of the specification does not define "homology". How does "homology" differ from identity? Does it mean that conservative or other types of amino acid substitutions are counted in the 65% homology or not counted?

Claim 19 lacks antecedent basis for the limitation "nucleic acid sequence according to any one of Claims 4 to 10" as claims 4-10 are drawn to a nucleic acid fragment.

Claim 21 is indefinite in its recitation of "adapted for the transformation of said host organism". The manner in which the selection marker is adapted is unclear. Has the coding sequence been modified or an unspecified extent or is the marker simply in an expression cassette?

Claim 27 remains indefinite because the step of regenerating a plant from a plant cell is not written in the gerund form. It is suggested that the phrase "a plant is regenerated from the plant cell" be replaced with --the method further comprises regenerating a plant from the plant cell--.

Claim 42 lacks antecedent basis for the limitation "the virus".

Claim Rejections - 35 USC § 102

13. Claims 4-6 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Kobayashi et al (1996, Genbank Accession No. D21812).

Kobayashi et al teach an isolated nucleic acid that encodes a protein of general formula (I), wherein Xab and Xad comprise at least one basic amino acid, which is lysine. This nucleic acid would be homologous to SEQ ID NO:1 because it contains one or more sequence modifications when compared to SEQ ID NO:1.

14. Claims 4 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Cheuk et al (1996, Genbank Accession No. AC003981).

Cheuk et al teach an isolated nucleic acid that encodes a protein, violaxanthin de-epoxidase, of general formula (I). This nucleic acid would be homologous to SEQ ID NO:1 because it contains one or more sequence modifications when compared to SEQ ID NO:1.

15. Claims 4-6 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Carlson et al (1996, Genbank Accession No. K02672).

Carlson et al teach an isolated nucleic acid that encodes a protein of general formula (I), wherein Xad comprises at least one basic amino acid, which is lysine. The protein is a ribonucleoside diphosphate reductase. This nucleic acid would be homologous to SEQ ID NO:1 because it contains one or more sequence modifications when compared to SEQ ID NO:1.

16. Claims 10, 19-30 and 41-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Maeda et al (1991, Virol. 184:777-780). The rejection is repeated for the reasons of record as set forth in the Office action mailed 22 April 2002, as applied to claims 1-10, 19-25, 28-29 and 39. Applicant's arguments filed 23 September 2002 have been fully considered but they are not persuasive.

Applicant urges that in light of the amendments to the claims, the protein taught by Maeda et al does not meet the formula in claim 4 and claims 7-8 (response pg 43-44).

This is not found persuasive because the nucleic acid encoding this protein would be homologous to SEQ ID NO:1 because it contains one or more sequence modifications when compared to SEQ ID NO:1.

Maeda et al teach a chimeric gene encoding a scorpion toxin AaIT; this nucleic acid would be homologous to SEQ ID NO:1 because it contains one or more sequence modifications when compared to SEQ ID NO:1. The chimeric gene functions in a baculovirus and is in an expression vector with a selection marker that is "adapted" to the host organism. Maeda et al also teach host organisms (*B. mori* cells) transformed with the vector via a baculovirus (pg 777, right column, paragraph 2). Lastly, Maeda et al teach a method of purifying the protein from the transformed host organism (pg 778-779).

17. Claims 10 and 19-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Ely (WO 95/11305). The rejection is repeated for the reasons of record as set forth in the Office action mailed 22 April 2002, as applied to claims 1-10, 19-32, 34 and 39. Applicant's arguments filed 23 September 2002 have been fully considered but they are not persuasive.

Applicant urges that in light of the amendments to the claims, the protein taught by Ely et al does not meet the formula in claim 4 and claims 7-8 (response pg 43-44).

This is not found persuasive because the nucleic acid encoding this protein would be homologous to SEQ ID NO:1 because it contains one or more sequence modifications when compared to SEQ ID NO:1.

Ely teaches a chimeric gene encoding the scorpion toxin AaHIT; this nucleic acid would be homologous to SEQ ID NO:1 because it contains one or more sequence modifications when compared to SEQ ID NO:1. The chimeric gene functions in a baculovirus and is in an

expression vector with a selection marker that is "adapted" to the host organism. Ely also teaches plants transformed with the vector (pg 9, paragraphs 1 and 4, and claim 7). The plants would be resistant to at least some fungal diseases because a pathogenic fungus cannot infect all plants. Lastly, Ely teaches a method of purifying the protein from the transformed host organism (paragraph spanning pg 7-8).

18. Claims 10 and 19-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Barton et al (1993, US Patent 5,177,308). The rejection is repeated for the reasons of record as set forth in the Office action mailed 22 April 2002, as applied to claims 1-10 and 19-35. Applicant's arguments filed 23 September 2002 have been fully considered but they are not persuasive.

Applicant urges that in light of the amendments to the claims, the protein taught by Barton et al does not meet the formula in claim 4 and claims 7-8 (response pg 43-44).

This is not found persuasive because the nucleic acid encoding this protein would be homologous to SEQ ID NO:1 because it contains one or more sequence modifications when compared to SEQ ID NO:1.

Barton et al teach a chimeric gene encoding the scorpion toxin AaIT; this nucleic acid would be homologous to SEQ ID NO:1 because it contains one or more sequence modifications when compared to SEQ ID NO:1. The chimeric gene functions in plants and bacteria and is in an expression vector with a selection marker that is "adapted" to the host organisms (column 9, lines 1-59). Barton et al also teach tobacco plants transformed with the vector (column 9, lines 44-59, and claims 1-2) and cultivation and crossing of the transformed plants (column 10, lines 37-52). Tobacco is resistant to at least some fungal diseases because a pathogenic fungus cannot infect all plants.

19. Claims 7-9 are free of the prior art, given the failure of the prior art to teach or suggest an isolated nucleic acid encoding a protein of the formula indicated in claim 7 or a nucleic acid encoding a protein with 65% identity to SEQ ID NO:2.

Conclusion

20. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Customer Service at (703) 308-0196.

Anne R. Kubelik, Ph.D.
January 16, 2003